Remarks/arguments

Claims 1 and 5-14 are pending. Claims 4 and 15 have been canceled. Claim 1 has been amended to incorporate the subject matter of claim 4. Claims 1 and 5-14 have been amended to recite that the transdermal administration of buprenorphine is by a transdermal patch. Support for the amendments can be found in the specification at paragraph 38. Dependent claims depending from claim 4 have been amended to depend from claim 1.

Rejections under 35 U.S.C. 102(b)

Claims 1 and 15 have been rejected under 35 U.S.C. 102(b) as anticipated by Fischer et al., Addiction, 2000;95(2):239-244. According to the Examiner, Fischer discloses a method of treating opioid dependent pregnant women with transmucosal buprenorphine tablets, and a transmucosal system is encompassed by the instant claims.

Applicants respectfully traverse this rejection. Claim 1 as amended is directed to transdermal delivery of buprenorphine by a transdermal patch. A transdermal patch is an across-the-skin drug delivery system which is not amenable to transmucosal delivery because such patches are not for application to mucosa. Thus, Fischer does not disclose the method of amended claim 1. Claim 15 has been canceled. Thus, this rejection should be withdrawn.

Rejections under 35 U.S.C. 103(a)

Claims 1 and 4-15 have been rejected under 35 U.S.C. 103(a) as obvious over EP 0432945 in view of Lintzeris et al., Drug and Alcohol Dependence, 2003;70:287-297, and Fischer. According to the Examiner, the '945 application discloses a transdermal buprenorphine dosage form comprising 0.25 – 100 mg of buprenorphine, which results in a blood plasma level of 0.6-6 ng/ml. The Examiner states that it would have been obvious to dose the patients of the

Lintzeris study with the transdermal formulation of the '945 application because oral and sublingual dosages only provide immediate relief of symptoms.

According to the Examiner, Lintzeris teaches a method of treating withdrawal symptoms in heroin-addicted patients by titrating different concentrations of transdermal buprenorphine formulations. The Examiner states that Fischer teaches the use of buprenorphine as a withdrawal treatment for pregnant women.

Applicants respectfully traverse this rejection. As stated above, Fischer discloses the use of sublingual buprenorphine to treat opioid-dependent pregnant women. Buprenorphine dosage amounts were variably titrated according to whether the patent was stabilized (Fischer, p. 240, right column) or upon patient request (Fischer, p. 240, right column). Lintzeris discloses the use of sublingual buprenorphine in "a symptom-triggered titration dosing regime" to treat heroin withdrawal. See, Lintzeris, abstract. The '945 application discloses the use of transdermal buprenorphine to treat heroin addiction.

According to the Examiner, "[o]ne of ordinary skill in the art would have been motivated to combine the prior art in order to properly and more effectively treat withdrawal symptoms." Office Action, p. 5. No reasoning is provided as to why (1) transdermal buprenorphine (i.e., a transdermal buprenorphine patch) would treat opioid dependence more "properly" than sublingual buprenorphine, or (2) transdermal buprenorphine (i.e., a transdermal buprenorphine patch) would "more effectively" treat opioid dependence compared to sublingual buprenorphine.

The instant claims are directed to a fixed dosage regimen for treating opioid withdrawal syndrome by administering a transdermal buprenorphine patch. Transdermal buprenorphine patches are for long term (i.e., days) use. The unpredictable and variable regimens taught by Fischer and Lintzeris discourage the use of such a dosage form. According to Fischer and

Lintzeris, the buprenorphine dose may change in a short time and at unpredictable intervals based on patient "stability," patient request, or patient symptoms. The sublingual tablets used in Fischer and Lintzeris are ideally suited for such regimens. See, e.g., '945 application, p. 3, ll. 2-5 (The half-life of the drug in the body after oral or sublingual administration is approximately three hours.). There would have been no motivation to replace the sublingual tablets of Fishcer and Lintzeris with a transdermal patch because the unpredictable and possibly frequent dosage changes would be wasteful of the longer-term patches, and repeated patch changes could result in skin breakdown.

The '945 application does not disclose or suggest an escalating dosage regimen or the treatment of pregnant women. An escalating dosage regimen as instantly claimed is important to increase the dosage rapidly in order "to achieve efficacy in as short a time as possible, while minimizing adverse effects of too high an initial dose of buprenorphine." Instant application, para. 24. A fixed transdermal patch dosage according to the '945 application runs the risk of too high an initial dosage. A too-high dosage may be particularly detrimental to a pregnant woman and her fetus. The '945 application does not recognize this patient population. Lintzeris and Fischer do recognize that the buprenorphine dosage may need to be increased. However, for the reasons stated above, the combined references teach that sublingual delivery is best suited for such a regimen, not a transdermal patch. Further, no combination of the references discloses the fixed, escalating dosage regimen of the instant claims.

For the reasons stated above, this rejection should be withdrawn.

Conclusion

This application is believed to be in condition for allowance. If any issues remain which may be addressed by an Examiner's amendment or a supplemental amendment, the Examiner is respectfully requested to contact the undersigned.

Respectfully submitted,

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